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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/166,649	Applicant(s) Schmidt et al.
	Examiner Eileen B. O'Hara	Group Art Unit 1646

X Responsive to communication(s) filed on *Jan 8, 2001*

This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

X Claim(s) *1-57* is/are pending in the applicat

Of the above, claim(s) *3, 9, 10, 14, 16, 19, 23, and 30-57* is/are withdrawn from consideration

Claim(s) _____ is/are allowed.

X Claim(s) *1, 2, 4-8, 11-13, 15, 17, 18, 20-22, and 24-29* is/are rejected.

Claim(s) _____ is/are objected to.

X Claims *1-57* are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-57 are pending in the instant application. Claims 1 and 18 have been amended as requested by Applicant in Paper Number 10, filed Jan. 8, 2001.

Claims 1, 2, 4-8, 11-13, 15, 17, 18, 20-22 and 24-29 are currently under examination.

Specification

2. The objection to the specification is maintained because the word "pepetide" on page 13, line 3, has not been corrected.

Withdrawn Rejections

3.1 The rejection of claims under 112 § 1 is withdrawn in view of Applicant's amendment.

3.2 The rejection of claim 18 under 112 § 2 is withdrawn in view of Applicant's amendment.

3.3 The rejection of claim 29 under 35 USC § 102(b) is withdrawn in view of Applicant's amendment.

3.4 The rejection of claims 11 and 12 under 35 USC § 103 is withdrawn in view of Applicant's amendment.

Claim Objections

4. Claim 11 is objected to because of the following informalities: "derivitive" should be spelled "derivative". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5.1 Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay using a peptide that is a carboxyl-lysine-modified AGE, does not reasonably provide enablement for a peptide derivative comprising an alkyl group. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

Claims 11 and 12 encompass the competitive binding assay of claim 1, in which the peptide derivative of step (a) (i) comprises an alkyl derivative, which can be an acetyl derivative, a propyl derivative, an isopropyl derivative, a butyl derivative, an isobutyl derivative, or a carboxymethyl derivative. The specification teaches a number of experiments that were performed to elucidate the specific binding of AGE peptides to a RAGE, or the effects of these AGE peptides on various cell types (Figures 1-7 and pages 4-6 of the specification). However, the only AGEs that were used in these experiments were carboxyl-lysine (CML), pentosidine, and methylglyoxal modified proteins. In Figure 1 and in the Brief Description of the Drawings on page 4 and the results section on pages 33-34, it was demonstrated that in the radioligand

binding assays in which CML-BSA, pentosidine-BSA or methylglyoxal-human serum albumin were tested, only CML-BSA specifically bound to RAGE. Both pentosidine-BSA and methylglyoxal-HSA did not bind specifically to RAGE. Similar results were found in the other experiments shown in Figures 2-7 and in the results section. There were no experiments performed with a peptide comprising an alkyl derivative. The prior art does not disclose that peptides comprising an alkyl derivative are AGEs, or that they would bind to RAGE.

It is not disclosed and not predictable from the limited teachings of the prior art and specification that a peptide comprising an alkyl derivative would bind to a RAGE and function in a competitive binding assay, as claimed. There is no guidance in the specification that such compounds would bind to RAGE, and the specification has not disclosed a single working example showing that such derivatives would bind. It is not predictable, based on the information provided in the specification or from the prior art, that the claimed compositions could be used in such assays, especially in light of the experimental results that teach that only the carboxymethly-lysine-modified peptide specifically bound to RAGE. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use a peptide comprising an alkyl derivative in the assay as claimed. Therefore, the method of using such derivatives is not enabled.

5.2 Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The step of admixing a peptide, Rage or a fragment thereof and a compound to be tested inside a cell, is critical or essential to the practice of the invention, but not included in

the claim and is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claim 29 requires that a competition assay for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay, comprises admixing the peptide with RAGE or a fragment of RAGE in the presence and the absence of the compound in a cell, which is interpreted to mean they are admixed inside the cell. The specification on page 9, lines 34-35, states "In another embodiment of the screening method, the admixing of step (a) occurs in a cell.", but there is no other information in the disclosure as to how these three components can be introduced into a cell nor how the amount of the peptide bound to the RAGE could be determined. It is not commonly practiced in the art that competition binding experiments are performed inside cells; however competition binding experiments in which one component is present on the outside of the cell are well known in the art. The specification has not taught the skilled artisan how to introduce these three components inside a cell in a manner in which they can freely interact and then determine the amount of binding, and the prior art has also not taught how to accomplish this type of assay. Therefore, claim 29 is not enabled for competition assays performed inside a cell.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-28 remain rejected under 35 U.S.C. 102(e) as being anticipated by Morser et al., PN 5,864,018, filing date April 16, 1996, for reasons cited in the previous Office Action, Paper No 9, at pages 6-8.

Claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-28 encompass a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay, and the reasons for rejection were discussed in the previous Office Action. Applicants traverse the rejection, and assert that Morser, et al. does not disclose every limitation of Applicant's claimed invention, and specifically does not describe that the amino groups of the peptide in the competition assay are inactivated by chemical derivatization. Applicants point out that "inactivated by derivatization" is described in Applicants' specification at page 12, as encompassing a chemical modification of a peptide so as to cause amino groups of the peptide to be less reactive with the chemical

modification than without such chemical modification. Applicants assert that Morser et al. does not disclose peptides so modified and therefore does not disclose Applicants' claimed method.

Applicant's arguments have been considered but are not found persuasive. Morser et al., in column 21, Example 2, describes the preparation of AGE-BSA, by incubating bovine serum albumin with ribose in the presence of PMSF. This is a chemical derivatization, and though Morser et al. does not specifically state that the amino groups of the BSA are less reactive with the chemical modification than without such chemical modification, this is inherent property of such a derivatized protein. Therefore, this modified peptide meets the limitations of the claims, and the rejection of claims under 35 USC § 102(e) is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 4 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Morser et al. and further in view of Reddy et al., Biochemistry, Vol.34, pp 10872-10878, 1995, for reasons cited in the previous Office Action, Paper No 9, at pages 9-10.

The rejection over claims 11 and 12 has been withdrawn because the prior art does not disclose a method for determining whether a compound is capable of inhibiting the interaction of

a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay using a peptide comprising an alkyl derivative. However, claim 4 remains rejected for the carboxymethly-lysine-modified peptides in the assay method.

Applicants argue on pages 16-17 that inhibiting one particular interaction between a particular peptide and RAGE does not enable one to accurately determine which potential compounds are capable of inhibiting the interaction of one or more of the many other potential peptide-RAGE combinations, and that one would therefore not be motivated based on the cited references to choose a particular peptide/RAGE interaction for which to determine which compounds might be capable of inhibiting that interaction. Applicants further assert that using the AGE described in Reddy in the method described in Morser, one would not arrive at the applicants' claimed invention because the method described in Morser does not include the limitations or steps recited in the claims of applicants' presently claimed invention, and therefore, applicants maintain that the Morser and Reddy references, either alone or in combination, do not render obvious applicant's claimed invention.

Applicants's arguments have been considered but are not found persuasive. Since Morser et al. teaches all of the steps and limitations of the assay with the exception of using carboxymethly-lysine-modified peptides in the assay method, and Reddy et al. teaches that carboxymethly-lysine is a dominant advanced glycation end product (AGE) antigen in proteins, and given that carboxymethyl-lysine-modified peptides are a dominant AGE, it would have been *prima facie* obvious to one of skill in the art of AGE/RAGE art at the time of the invention to use

a carboxymethly-lysine-modified peptide of Reddy as the AGE in the AGE/RAGE competition assay of Morser et al. to determine whether a compound is capable of inhibiting the AGE/RAGE interaction. Therefore, the rejection of claim 4 under 35 U.S.C. 103(a) is maintained. By

It is believed that all pertinent arguments have been answered.

Conclusion

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER